REMARKS

Claims 1, 2, 7-18, 20-28, 33-44, and 47-55 were pending in the instant application. By the present communication no claims have been added or cancelled, and claims 1 and 26 have been amended. The amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 1, 2, 7-18, 20-28, 33-44, and 47-55 are currently pending in this application.

The Sequence Listing

Applicants respectfully traverse the assertion that this application fails to comply with the requirements under the sequence rules, 37 CFR 1.821-1.825. Applicants submitted the paper copy for inclusion in the subject application, along with the letter stating that the contents of the computer readable format (CRF) and the sequence amendment are the same, on January 18, 2002 (a copy of which is herein attached). However, to expedite prosecution of the subject application, Applicants submit herewith a paper copy of the Sequence Listing for the above-identified application. The paper copy of the Sequence Listing in this application is identical to the computer readable copy of the Sequence Listing filed in U.S. Patent Application Serial No. 08/876,276 filed June 16, 1997. In accordance with 37 C.F.R. § 1.821(e), please use the computer readable form filed with that application as the computer readable form for the instant application. The specification has been amended to insert the paper copy of the Sequence Listing.

Applicant hereby states, as required by 37 C.F.R. 1.821(f), that, except for the priority information, the content of the paper copy of the Sequence Listing in the present application is identical to the computer readable copy of the Sequence Listing filed in U.S. Serial No. 08/876,276, filed June 16, 1997, and that the submission filed herewith in accordance with 37 C.F.R. 1.821(g) does not include new matter.

The Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1, 2, 7-18, 22-28, 33-44, and 50-55 are rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter. Claims 1 and 26 have been amended to insert an additional term "myceliate" to limit fungi. Furthermore, claims 1 and 26 were amended to bring the number of bacteria and fungi into grammatical agreement, as suggested by the Examiner. Thus, Applicant submits that grounds for the rejection of claims 1, 2, 7-18, 22-28, 33-44, and 50-55 for lack of clarity are overcome, and reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection under 35 U.S.C. §103(a)

Claims 1, 2, 7-18, 23-28, 33-44, and 51-53 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Thompson et al. ('485) in view of Plovins et al. and Zhang et al. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1468 (Fed. Cir. 1991). The mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Applicants respectfully traverse the rejection of claims 1, 2, 7-18, 23-28, 33-44, and 51-53 under 35 U.S.C. 103(a) as allegedly being unpatentable over Thompson et al. (hereinafter

"Thompson") in view of Plovins et al. (hereinafter "Plovins") and Zhang et al.(hereinafter "Zhang"). Applicants respectfully submit that the invention methods for identifying bioactivities or biomolecules using high throughput screening of nucleic acid, as defined by amended claims 1 and 26, distinguish over the combined disclosures of Thompson, Plovins and Zhang, at least by reciting:

> generating an environmental gene library containing a plurality of clones in E.coli, wherein the nucleic acid for generating the library is naturally occurring and obtained from a mixed population of uncultured organisms; transferring a plurality of the clones to myceliate bacteria or myceliate fungi; encapsulating a bioactive substrate and at least one transferred clone in a gel microdroplet, wherein a bioactivity or biomolecule produced by the clone is detectable by a change in fluorescence of the substrate prior to contacting with the at least one clone as compared to after the contacting; and screening the microdroplet with an assay or an analyzer that detects the presence therein of the change in fluorescence of the substrate, wherein the change indicates the identity of the bioactivity or biomolecule.

As noted by the Examiner on Page 3 of the instant Office Action, claim 1 (as well as claim 26) was amended to include an additional step b), drawn to the step of transferring a plurality of the clones to a myceliate bacteria or fungi. As further noted by the Examiner, Thompson teaches the use of 2 *Strepomyces* species, *Neurospora crassa* or *Aspergillus nidulans* as host cells for the clones. Applicants' invention, as described by amended claims 1 and 26, involve use of two distinct host cells to identify a bioactivity or biomolecule. In contrast, Thompson describes a plethora of preferred host organisms at column 18, lines 45-56. However, the teachings of Thompson do not directly teach, or even suggest that the transfer of clones from a first host cell to a second host cell will effect production of, or identify, biomolecules or bioactivities.

Plovins fails to cure the deficiencies in Thomson. The Examiner relies upon Plovins as disclosing use of FDG as well as C_{12}FDG as substrates in animal, bacterial and yeast cells. Applicants rely upon arguments of record set forth in Papers Nos. 5, 13, and 17, and note that Plovins further does not teach the transfer of clones to a second host cell. Thus, Applicants respectfully submit that the combined disclosures of Thompson and Plovins fail to teach or suggest the invention methods for identifying bioactivities or biomolecules using high throughput screening, as defined by amended claims 1 and 26.

Like Plovins, Zhang also fails to cure the deficiencies of Thompson for teaching or suggesting the invention methods for identifying bioactivities or biomolecules using high throughput screening, as defined by amended claims 1 and 26. The Examiner relies upon Zhang for disclosure of the development of lipophilic, fluorogenic substrates derived from FDG, such as FDG having an added lipophilic tail, to enable the substrate to pass through the cellular membrane. Applicants rely upon arguments of record set forth in Papers Nos. 5, 13, and 17, and similarly note that Zhang does not teach the transfer of clones to a second host cell.

In view of the failure of either Plovins or Zhang to cure the above-identified deficiencies of Thompson for suggesting the invention methods, Applicants respectfully submit that the combined disclosures of Thompson, Plovins, and Zhang are not sufficient to teach or suggest the present invention under 35 U.S.C. 103, and reconsideration and withdrawal of the rejection is respectfully requested.

In view of the above amendments and remarks, reconsideration and favorable action on claims 1, 2, 7-18, 20-28, 33-44, and 47-55 are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative, can be reached at (858) 526-5176.

Respectfully submitted,

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